

been reported that oral delivery of DNA encapsulated in poly-lactide-co-glycolide (PLG) microspheres can generate immune responses against rotavirus infections. Oral gene delivery for correcting lactose intolerance in a rat model has also been achieved using an adeno-associated-viral vector⁴⁵. Chitosan is an attractive oral gene carrier because of its reported adhesive and transport properties in the gut. Furthermore, chitosan, when complexed with pDNA, can form stable nanoparticles that can be endocytosed by cells in the gastro-intestinal tract. Chitosan being a mucoadhesive polymer, the DNA-nanoparticles might adhere to the gastro-intestinal epithelia, transported across the mucosal boundary by M-cells and transect epithelial and/or immune cells in the gut associated lymphoid tissue either directly or through "antigen transfer", as suggested by the β -galactosidase expression following chitosan-p43LacZ delivery. In vitro studies have also shown that chitosan can enhance trans and pericellular transport of drugs across intestinal epithelial monolayers.

The anaphylaxis response in nanoparticle-immunized mice indicates that significant protection can be achieved against allergen challenge by oral delivery of a single dose of plasmid DNA in particle formulation. Unfortunately, the results of a single booster administration were inconclusive indicating that further studies are necessary to investigate the effect of multiple doses and kinetics for an optimal vaccination protocol. The level of plasma histamine in the booster group following challenge would not have suggested anaphylactic protection. The fact that same degree of protection was still observed suggests that the pathogenesis of allergic anaphylaxis in this murine model may be multifactorial.

While the above examples utilize an IgE response to demonstrate principle, this is but one example of a useful response elicited against an antigen. Any type of immune response may be modified by oral vaccination using the nanospheres as taught herein.

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